REMARKS

The present invention is directed to compositions and methods for the oral vaccination of healthy animals through drinking water or syrups as an aid in the prevention of disease, and is particularly applicable compositions and methods for mass vaccination.

35 U.S.C. § 112 Rejection – Maintained

The Examiner maintained the February 14, 2003 rejection of claim 3, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, claim 3 continues to be rejected for vagueness and indefiniteness in the use of the abbreviated recitation of "PRRS" in the claim language.

Applicants submit that with the hereinabove amendment to claim 3, reciting that PRRS virus, an abbreviation well known in the art represents Porcine Reproductive and Respiratory Syndrome virus has now traversed this 112 rejection, and doe not represent new matter. Withdrawal of this rejection is therefore respectfully requested.

35 U.S.C. § 112 Rejection – New

The Examiner rejected claim 3, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In particular, claim 3 has been rejected for being incorrect and confusing in the recitation of "choleraeusis" in the claim language.

The spelling has now been corrected, and, accordingly, this rejection has also been traversed, and, the withdrawal of this rejection is also respectfully solicited.

35 U.S.C. § 103 Rejections

1. Claims 1, 29 and 30

Claims 1, 29 and 30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Heo *et al.* (US 6, 491, 956, already of record) in view of DE patent 1793631, Shimada *et al.* (US 5,626,837) and Cederholm-Williams (US 2002/0064517 A1). Heo *et al.*, the primary reference, is cited as disclosing a food for human consumption that contains an active strain of a non-toxic living microorganism being either *Lactobacillus acidophilus* HY2177 or *Lactobacillus casei* HY 2743. The food containing the microorganism is delivered in a drinkable yogurt, buttermilk, cream cheese or ice cream nutritional vehicle. The *Lactobacillus* is introduced into the stomach for the purpose of colonizing the gut thereby inhibiting the attachment of *Helicobacter pylori* (*H. pylori*) to gastric mucosal cells, resulting in the inhibition of urease and Interleukin-8 production. The Office has stated that the "human" described in Heo *et al.*, in view of Cederholm-Williams, qualifies as a mammalian animal. Although Heo *et al.* is silent about the use of a flavorant, the Office states that use of a flavorant in Heo *et al.*'s bacterial composition was well known in view of DE 1793631 and Shimada *et al.* Specifically, the Office states that the DE 1793631 teaching of an ice cream, yogurt and milk drink with a strawberry flavorant implicitly discloses a water soluble flavorant, which was known in the art because of Shimada *et al.*, which taught a water soluble strawberry flavorant.

Applicants respectfully disagree.

The essential teaching of Heo to those skilled in the art is of a nutritional formulation in the form of a foodstuff, a formulation/foodstuff in which bacteria which is non-toxic to humans thrive, and in which, optionally and preferably, the prophylactic and/or therapeutic effects of the comestible bacteria are boosted with egg yolk containing immunoglobulins specific to *H. pylori*. The rejection suggests that the

"human" in Heo qualifies as an animal and is implicit from what is well known in the art, and moreover, that flavorants are also known in the art as can be observed from the secondary references.

This construction of the references is improper and ignores the specific teachings of the references, and the context of those teachings. What is appropriate for a nutritional foodstuff directed to a human is not in anyway analogous to a non-foodstuff, non-nutritional vaccine and a method of oral vaccination for non-humans. Moreover, there is a vast difference, as it relates to oral vaccination, between a human and an animal. Thus, whether or not, a human qualifies as an animal, and particularly a non-human animal, is beside the point; just as, whether or not, it would be obvious to add a flavorant to a foodstuff or the bactericidal, oral, gargle composition is beside the point. The rejection selectively negates the "human" directness of Heo, elects to ignore nutritional inclusiveness of Heo and what and how that would affect the presence of live antigens in the vaccine, and, also excludes the presence of a bactericide of one of the secondary references and how would impact the antigens in the vaccine and their administration.

Consequently, Heo, alone or in combination with any of the De patent, Shimada or Cederholm-Williams do not make obvious the invention defined by the method of claims 1, 29 and 30. Applicants therefore request that said obviousness rejection be withdrawn.

2. Claims 1-3, 5, 6, 29 and 30

Claims 1-3, 5, 6, 29 and 30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Casas *et al.* (US 6, 100, 388, already of record) in view of DE patent 1793631 and Shimada *et al.* (US 5,626,837). Casas *et al.* is cited as describing a Lactobacilli vaccine, which expresses an *E. coli* antigen, that can be delivered by use of a pharmaceutically acceptable carrier or it can be added to milk or milk products, *e.g.*, yogurt. Although Casas *et al.* is silent about the use of a flavorant, the Office states that use of a flavorant in Casas *et al.*'s Lactobacilli vaccine was well known in view of DE 1793631 and Shimada *et al.* Specifically, the Office states that the DE 1793631 teaching of an ice cream, yogurt and milk drink with a strawberry flavorant implicitly discloses a water soluble flavorant, which was known in the art because of Shimada *et al.*, which taught a water soluble strawberry flavorant.

The central teaching of Casas as the primary reference is of a vaccine prepared from live Lactobacillus cells which have been transformed ... to express heterologous antigens. The transformed Lactobacillus, which are generally non-toxic, and as constructed has the ability to adhere to mucosal surfaces of the gastrointestinal tract where lactobacilli thrive. The use of lactobacillus as a vaccine vehicle, for oral or intranasal vaccination, is the context of Casas, and excludes other vaccine vehicles or other forms of antigen delivery. Because Casas relates to Lactobacillus there is, arguably, a natural extension to it being added to a milk or milk product for delivery because it is naturally present in milk and milk products, but there is no such "obvious" connection or extension to other forms of oral vaccination. Moreover, combining the teaching of Casas to the bactericidic composition of Shimada for example, would therefore be contraindicated. Accordingly this combination of references and whether or not, in this context, it is appropriate or obvious to add a flavorant to a milk product is the antithesis of obviousness.

Consequently, Shimada *et al.* does not support DE 1793631, which itself, in view of Casas *et al.*, does not render the present invention prima facie obvious.

Applicants therefore respectfully that this obviousness rejection should also be withdrawn.

3. Claims 1-3, 5, 6, 29 and 30

Claims 1-3, 5, 6, 29 and 30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Clements *et al.* (US 6, 019, 982, already of record) in view of DE patent 1793631 and Shimada *et al.* (US 5,626,837). Clements *et al.* is said to disclose an oral vaccine preparation with an *E. coli* antigen that may be reconstituted in buffered saline, milk, or any other physiologically compatible medium. *See* Clements *et al.* '982 patent at section 5.2, column 14, line 39. Although Clements *et al.* is said to be silent about the use of a flavorant, the Office states that use of a flavorant in Clements *et al.*'s *E. coli*-containing oral vaccine was well known in view of DE 1793631 and Shimada *et al.* Specifically, the Office states that the DE 1793631 teaching of an ice cream, yogurt and milk drink with a strawberry flavorant implicitly discloses a water soluble flavorant, which was known in the art because of Shimada *et al.*, which taught a water soluble strawberry flavorant. Applicants disagree.

The core teaching of Clements, however, is to the use of mLT as an adjuvant with a biologically relevant, orally administered, antigen and/or vaccine, to increase mucosal immune response. For this purpose, Clements discloses the vaccinal preparation, may be liquid or solid; may be in the form of tablets, capsule, powders, granules, suspensions or solutions; and may be reconstituted or suspended in milk or other pharmaceutical vehicle; and may contain any of the other components in which any of these listed forms of delivery are typical. Such a kitchen cabinet type listing/disclosure does not make obvious, it is submitted, the invention defined by the method of claims 1-3, 5, 6, 29 and 30. Nor is the invention made obvious to one skilled in the art, by the disclosures of Shimada, because the references provide no suggestion as how this combination leads to the instantly claimed invention.

Withdrawal of this 35 U.S.C. § 103(a) obviousness rejection is therefore respectfully requested.

4. Claims 4, 7, 27 and 28

Claims 4, 7, 27 and 28 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Casas *et al.* (US 6, 100, 388, already of record) or Clements *et al.* (US 6, 019, 982, already of record) as modified by the DE patent 1793631 and Shimada *et al.* (US 5,626,837), as applied to claims 1 and 4, and further in view of Greive (Poultry Digest, November 1992, pp. 28-32, already of record). The Office states that although the teachings of Casas *et al.* or Clements *et al.*, as modified by the DE 1793631 and Shimada *et al.* as explained in the Examiner's rejections above, do not disclose the administration of the vaccine through drinking water that it was routine to carry out mass vaccination of poultry via drinking water at the time of the present invention. Specifically, the Office states that Grieve's teaching of mass vaccination of poultry via drinking water renders Casas *et al.*'s or Clements *et al.*'s vaccinations, as modified by DE 1793631 and Shimada *et al.*, known at the time of the present invention. Applicants strongly disagree.

Grieve does not add to the combination of references already discussed in the prior two rejections without Grieve. In each case, the rejection posits a view of the art that together lists multiple components and suggests that these components, because they are known in their various contexts, make the claimed invention obvious. This selective reading if the art, has never been found to form the basis of a proper 103 rejection, absent a direction in the art that leads to the invention. That direction or

suggestion is absent from Clements and Casas, is not remedied by Shimada, and is not supplied by Grieve's use of a blue dye.

Applicants therefore submit that the rejection, based on the addition of Grieve to the previously cited references, does not make obvious the invention of defined by claims 4, 7, 27 and 28, to those skilled in the art. Withdrawal of the 35 U.S.C. § 103(a) rejection is therefore respectfully requested.

5. Claim 10

Claim 10 was also rejected under 35 U.S.C. § 103(a) as being unpatentable over Casas *et al.* (US 6, 100, 388, already of record) or Clements *et al.* (US 6, 019, 982, already of record) as modified by the DE patent 1793631, Shimada *et al.* (US 5,626,837) and Greive (Poultry Digest, November 1992, pp. 28-32, already of record) as applied to claims 1, 6 and 7, and further in view of Roland (US 6,399,074, already of record). The Office states that the teachings of Casas *et al.*, Clements *et al.* and Grieve, as explained in the previous rejections of the Final Rejection Office Action (above), do not disclose administering the vaccine into the mouth through a syringe. The Office states, however, use of a syringe for oral vaccination of birds was routine at the time of the invention in light of the Roland reference.

Applicants respectfully traverse the 35 U.S.C. § 103(a) obviousness rejection.

The addition of Roland again adds no disclosure teaching that makes obvious how the addition of a flavorant to a syringe administered oral vaccine, makes obvious claimed method of providing protection against disease. It is yet another reference that merely lists something in common with a feature of the claimed invention but does not teach or suggest to one skilled in the art the invention defined by claim 10. Withdrawal of this 35 U.S.C. § 103(a) rejection is therefore also respectfully requested.

6. Claim 8

Claim 8 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Clements *et al.* (US 6, 019, 982, already of record) as modified by the DE patent 1793631, Shimada *et al.* (US 5,626,837) and Greive (Poultry Digest, November 1992, pp. 28-32, already of record) as applied to claims 1, 6 and 7, and further in view of Frantz *et al.* (US 5,536,496, already of record). The Office states that the teachings of Clements *et al.*, as modified by DE 1793631, Shimada *et al.* and Grieve, as explained in the previous rejections of the Final Rejection Office Action (above), does not disclose administering a Erysipelothrix rhusiopathiae-containing vaccine. The Office states, however, that Clements *et al.* taught the vaccine may contain any biologically relevant pathogen or virulence determinants of specific pathogens, and that Frantz *et al.* disclosed use of Erysipelothrix rhusiopathiae bacterin or vaccine, suitable for any mode of administration. The Office states that it would have been obvious at the time of the present invention to use Frantz's Erysipelothrix rhusiopathiae bacterin or vaccine in Clements' method as modified by DE 1793631, Shimada *et al.* and Grieve.

Applicants disagree.

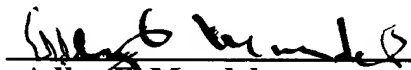
As before, the citation of a reference, Frantz, to identify a particular antigen does not make obvious the invention defined by the method of claim 8. The Frantz teaching of a new *P. multocida* protein or that it can be combined with *E. rhusiopathiae* antigen hardly qualifies as a teaching motivating the production of the invention. Respectfully, this amounts to hindsight, and equates the disclosure of any specific component in the art in general with motivation. Motivation, and the suggestion to combine, to arrive at the invention claimed, must be shown to come

from the references. The rejection fails to make the *prima facie* case, and, accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection is respectfully requested.

Reconsideration of this application and the rejection of all pending claims is respectfully requested, and the issuance of a Notice of Allowance is earnestly solicited. A petition for extension of time and Notice of Appeal are found other papers submitted with this correspondence.

Because the number of claims has not been changed by this response, the response is not accompanied by a transmittal letter. If any additional fees are required by this response or the accompanying papers, the Patent Office is authorized to charge such fees to Deposit Account No. 01-1425.

Respectfully submitted,



Adley F. Mandel
Attorney for Applicants
Reg. No. **26,942**

Wyeth
Patent Law Department
Five Giralda Farms
Madison, NJ 07940
Tel. No. (973) 660-**7659**